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## Functional brain laterality in adulthood ADHD

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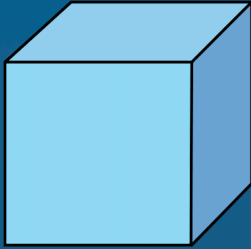
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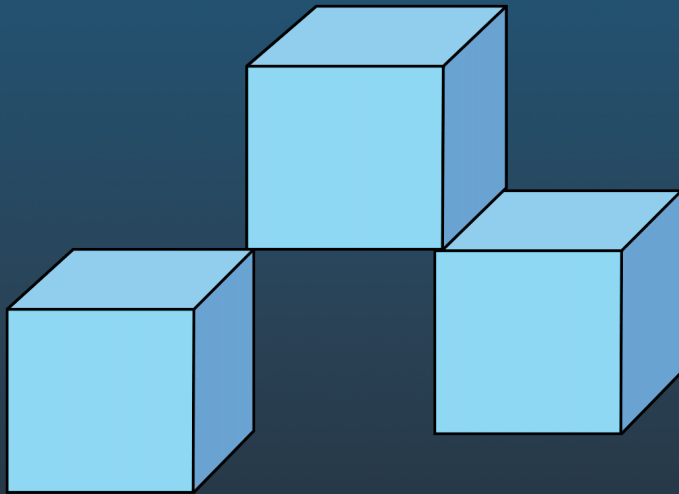
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## Chapter 4

**Linking state regulation, brain laterality, and self-reported attention-deficit/hyperactivity disorder (ADHD) symptoms in adults. (study 3)**



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Mohamed, S. M., Börger, N. A., Geuze, R. H., & van der Meere, J. J. (2016). Linking state regulation, brain laterality, and self-reported attention-deficit/hyperactivity disorder (ADHD) symptoms in adults. *Journal of clinical and experimental neuropsychology*, 38 (8), 831-843. (Published)

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### Abstract

**Purpose:** Many clinical studies have shown that performance of subjects with Attention Deficit Hyperactivity Disorder is impaired when presenting stimuli in a slow rate compared to a medium or fast rate. According to the cognitive-energetic model, this finding may reflect difficulty in allocating sufficient effort to regulate the motor activation state. Other studies have shown that the left hemisphere is relatively responsible for keeping humans motivated, allocating sufficient effort to complete their tasks. This leads to a prediction that poor effort allocation might be associated with an affected left hemisphere functioning in ADHD. So far, this prediction has not been directly tested which is the aim of the present study.

**Method:** Seventy-seven adults with various scores on the Conners' Adult ADHD Rating Scale performed a lateralized lexical decision task in three conditions with stimuli presented in a fast, a medium, and a slow rate. The left-hemisphere functioning was measured in terms of visual field advantage (better performance for the right than for the left visual field).

**Results:** All subjects showed an increased right visual field advantage for word processing in the slow presentation rate of stimuli compared to the fast and the medium rate. Higher ADHD scores were related to a reduced right visual field advantage in the slow rate only.

**Conclusions:** The present findings suggest that ADHD symptomatology is associated with less involvement of the left hemisphere when extra effort allocation is needed to optimize the low motor activation state.

## Introduction

The cognitive-energetic model, originally developed by Sanders (1983, 1998), has attracted much interest in the field of attention-deficit/hyperactivity disorder (ADHD: DSM V). The advantage of this model is that it addresses one of the most basic questions: is poor task performance in subjects with ADHD due to impaired cognition or poor motivation? The model combines elementary cognitive information processes with motivation (effort allocation) needed to control arousal (a phasic physiological response to stimuli processing) and motor activation (a tonic readiness for action). The definitions of these basic concepts are grounded on the seminal work of Pribram and McGuinness (1975) and have been recently adopted to value the conceptualization of arousal, activation and effort as distinct energetic aspects in physiological and psychological research (Damanpak, Mokhtari, & Mousavi, 2014; Sabzi, Roozbahani, & Hasanvand, 2012; Vaezmousavi, Barry, Rushby, & Clarke, 2007).

Applying the cognitive-energetic model in clinical research has revealed that subjects with ADHD perform well and do not differ from controls when stimuli are presented in a medium rate, but they show a decline in performance compared to controls during a fast and slow presentation rate of stimuli. According to the model, fast and slow presentation rate of stimuli affect the motor activation state of the subjects which leads to a decline in the performance on a variety of cognitive tasks, including Stop Signal Tasks, Go/No-Go tasks, Continuous Performance Task, memory tasks, delay aversion tasks, and learning tasks (Epstein et al., 2011; van der Meere, Shalev, Börger, & Gross-Tsur, 1995; for a review see also, van der Meere, 2005). To maintain the performance, subjects must allocate extra effort to regulate and optimize their activation state to fulfil task demands (for a meta-analysis see, Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012). Studies using psychophysiological measures of effort allocation, such as P300 and heart rate, have indicated that subjects with ADHD do not allocate sufficient effort to the task especially during the slow presentation rate (Buyck & Wiersema, 2014; Sergeant, 2005; Sergeant, Geurts, Huijbregts, Scheres, & Oosterlaan, 2003; Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010; van der Meere, Börger, & Wiersema, 2010). Therefore, it is concluded that subjects with ADHD have no deficit in elementary cognitive processes per se, but allocate insufficient effort/energy to regulate their psycho-physiological motor activation state. In the time of Sanders, the term extra energy allocation was merely used as a metaphor and was not intended to refer to physical energy. Nowadays, the cognitive-energetic model and its term energy allocation has been linked with inadequate lactate supply, which is a crucial fuel for the neuron especially in ADHD (Killeen, Russell, & Sergeant, 2013).

It is surprising that the state regulation deficit hypothesis in ADHD has not yet been investigated from the perspective of brain laterality since arousal and motor activation states, the neuro-energetic components of task performance, are related respectively to the right and the left hemisphere functioning (Declerck, de Brabander, & Boone, 2004; Friedman & Förster, 2005; Heilman, 1995; Petersen & Posner, 2012; Tucker & Williamson, 1984). The right midbrain regulates the arousal via noradrenergic pathways, while the left hemisphere regulates the motor activation via dopaminergic neurons (Alfano & Cimino, 2008; Derryberry & Rothbart, 1997; Heller, Nitschke, & Lindsay, 1997; Luu, Tucker, & Derryberry, 1998). Consequently,

the assumed deficit in regulating the motor activation state in subjects with ADHD might be associated with impaired left hemisphere functioning. Further evidence that poor state regulation is connected to the left hemisphere functioning in ADHD comes from fMRI studies. Raichle et al. (2001) proposed the existence of two anti-correlational brain networks: the positive task network which becomes active when the subject is motivated to carry out a task, and the default mode network (DMN) which becomes active when the subject becomes demotivated; this was later supported by other fMRI studies (Broyd et al., 2009; Fassbender et al., 2009; Liddle et al., 2011). It has been found that ADHD is associated with increased DMN activity especially in the left hemisphere during cognitive performance (Hale et al., 2014; Metin et al., 2015). In particular, the study by Metin et al. (2015) is of interest here as it investigated the DMN activity during fast, medium and slow presentation rate of stimuli using a go/no-go task. In this study, more activity was found in the left-lateralized DMN areas during the slow presentation rate.

Unfortunately, the fMRI studies did not report the behavioural consequences of the observed atypical left hemisphere activity during state regulation. One way to explore the behavioural consequences of the assumed abnormal left hemisphere functioning during different conditions of state regulation in ADHD, is to combine a lateralized lexical decision task with the presentation rate manipulation (tapping the motor activation state). The reason is that the lateralized lexical decision task has a wide tradition to study left hemisphere functioning at the behavioural level. Here, task performance reflects structural and functional brain asymmetry such as more activity in Broca's region (area 44, 45) and low fractional anisotropy values in the white matter of inferior parietal and frontal language area (Gold, Powell, Xuan, Jiang, & Hardy, 2007; Heim, Wehnelt, Grande, Huber, & Amunts, 2013; Hunter & Brysbaert, 2008; Mohr et al., 2005; Perea & Fraga, 2006; Price 2010; van Strien & van Kampen, 2009).

The lexical decision task used in the present study measures the ability to process words and non-words by presenting a target on either the Right Visual Field (RVF) or the Left Visual Field (LVF) while another stimulus (the distracter: word or non-word) is projected to the opposite visual field. Based on the fact that stimuli of one visual field are processed by the contralateral hemisphere (RVF stimuli are initially processed by the left hemisphere and LVF stimuli are initially processed by the right hemisphere) the task provides an index of the functional asymmetry between the two hemispheres by calculating the difference between LVF and RVF stimuli in reaction time performance. Typically, right-handed subjects show faster and more accurate performance for word stimuli when presented in the RVF. The RVF advantage for words is taken to reflect left hemisphere specialization in word recognition and written language (Jordan, Patching, & Milner, 2000).

In the present study, the lexical decision task is carried out during a fast, medium and slow stimulus presentation rate that respectively induces over-, medium-, and under- motor activation states. Given the fact that the abovementioned studies have shown that: (a) ADHD performance declines when the motor activation state is affected, (b) the left hemisphere is responsible for regulating the motor activation state, and (c) subjects with ADHD have a reduced task related activity in the left hemisphere during slow presentation rate of stimuli, we assume that ADHD is associated with an affected left hemisphere functioning during

state regulation. If so, the RVF advantage for words (faster and more accurate responses) will decrease in the fast and slow rate compared to the medium rate in subjects with high level of ADHD symptoms. It is obvious that while testing the involvement of the left hemisphere during state regulation, a so-called control condition is needed to measure the involvement of the right hemisphere. Research has indicated that non-words are processed equally in both hemispheres or even more accurately in the right hemisphere, and that high-frequency words are processed better than low-frequency words in the right hemisphere (Hale et al., 2005; Voyer, 2003). From this perspective, it may be hypothesized that if the right hemisphere is compromised during state regulation in ADHD then subjects with high level of ADHD symptoms would show slow and less accurate processing in the LVF for non-words and high-frequency words.

The expectations of the present study are tested using the dimensional approach. There is increasing interest in studying ADHD as a dimensional trait rather than as a disorder (Hudziak, Achenbach, Althoff, & Pine, 2007). Normal subjects report varying degrees of ADHD problems on scales used to measure clinical deficits such as the Conners' Adult ADHD Rating Scale (CAARS: Conners, Erhardt, & Sparrow, 1999). Thus, in the population the scale scores will be continuous and adults scoring at the high end of these scales might be diagnosed with ADHD. Here, we propose that level of self-reported ADHD problems in daily life activities is related to brain laterality and state regulation capacity. In the present study, participants were university students. A university student population was chosen because comorbidities, which are often present in clinical cases with ADHD (such as conduct disorder and learning disabilities) are rare in such a student population. Moreover, together with a narrow age range, the level of IQ and other demographic variables are expected to be relatively homogeneous across the sample. These factors are well recognized to confound outcomes of ADHD research.

Participants completed the CAARS (Conners et al., 1999). The scale is well validated (Adler et al., 2008; Erhardt, Epstein, Conners, Parker, & Sitarenios, 1999) and has been often used to assess clinical symptoms of ADHD (Dillo et al., 2010; Solanto et al., 2014). Moreover, CAARS scores are associated with ADHD pathophysiology such as the dysfunction of neurotransmission (Volkow et al., 2007, 2011) and dysfunctional fronto-parietal circuits (Sebastian et al., 2012). Briefly, the present study aims to test whether the left hemisphere functioning during state regulation is associated with the level of ADHD symptomatology.

## Method

### Participants

Eighty-four right-handed university students were recruited from the university of Groningen to participate in the study. Seven students were excluded as they had a score above seven on the inconsistency index of the CAARS that purported to identify random or careless responding. The participating sample was 77 students (38 males, 39 females) with mean age of 21.37 ( $SD = 2.89$ ,  $min: max = 18: 31$ ) years. Handedness was measured by the Edinburgh Handedness Inventory (Oldfield, 1971), the participants were right-handed ( $M = 80$ ,  $SD = 20.7$ ,  $min: max = 20: 100$ ). They reported (1) normal or corrected to normal vision, (2) no motor or learning

disorders, (3) no use of medication within at least 24 hours before their participation, and (4) either Dutch or German as a mother language. Sixteen participants reported a current ADHD diagnosis, and 4 participants reported a childhood ADHD diagnosis. The Ethics Committee Psychology of the University of Groningen approved the study (research code “14026-NE”). Participants were informed that their responses will be kept strictly confidential and anonymous, and they have the option to withdraw from the study at any time, without penalty. Thereafter, participants signed the informed consent for their participation in the study.

### Materials and apparatus

The experiment was conducted on a laptop computer using E-Prime software version 2.0. The visual stimuli were displayed on a 15.6 inch LED anti-glare monitor with a screen resolution of  $1024 \times 768$  pixels and a refresh rate of 60 Hz. Stimuli were presented in black colour on a silver background. Participants were seated in a comfortable posture with their head on a chin-rest 57 cm away from the monitor. A response box with two buttons was positioned halfway between the monitor and the chin rest.

The Conners' Adult ADHD Rating Scale (CAARS; Conners et al., 1999) was used to measure self-reported ADHD symptoms. The scale assesses four areas of impairment: three domains of ADHD identified by DSM-IV (inattention, hyperactivity, and impulsivity), and a fourth component measuring problems with self-concept. Based on eight pairs of items, an inconsistency index was calculated that indicates inconsistent responding on the CAARS. In addition, the CAARS contains the ADHD index subscale that provides a method to identify adults who are likely to be diagnosed with ADHD (Conners et al., 1999; Hudziak, Derks, Althoff, Rettew, & Boomsma, 2005). Participants filled in the entire questionnaire, but the ADHD index subscale was the main measure of interest in the data analysis because according to the manual, the scale is considered to be the most reliable and valid sub-scale to measure the overall ADHD symptomatology. The subscale consists of 12 items covering the four areas of ADHD impairments. Participants were asked to rate themselves for the items on a 4-point scale ranging from “0” (Not at all/Never) to “3” (Very much/Very Frequently). Figure 3.1. illustrates the distribution of T-scores on the ADHD index subscale. According to the manual of the CAARS, a T-score  $> 65$  can be used as a clinical cut-off indicating clinically significant problems in those presenting to a mental health clinic. A higher score (e.g., T-score of 70 or even 75) can be used to infer clinically significant problems in populations without identified problems.

A lateralized lexical decision task was used to measure left hemisphere function. In the task, participants had to indicate whether a target stimulus presented to the LVF or RVF was a word or a non-word while another stimulus (the distracter: word or non-word) was projected into the opposite visual field. We chose bilateral visual presentation because, compared to unilateral presentation, the bilateral presentation maximizes hemispheric independence in performing the lexical decision task (see, Fernandino, Iacoboni, & Zaidel, 2007; Iacoboni & Zaidel, 1996). The target letter-string was indicated by an underscore, and presented equally frequently in both visual fields. Since Dutch and German students participated in the study, the stimuli were presented in Dutch or German correspondingly. The presentation ratio



of word and non-word was 50:50 per visual field for Dutch and German language. Half of Dutch and German words had a high frequency (greater than 100 per million). The other half had a low frequency (less than 50 per million). High and low frequency words of Dutch and German language were assessed separately and both derived from two databases: the CELEX (Baayen, Piepenbrock, & Gulikers, 1995) and the SUBTLEX (Brysbaert et al., 2011; Brysbaert & New, 2010). To ensure that stimuli were processed lexically in the left hemisphere, non-words consisted of pronounceable syllables corresponding with syllables of the target words. The pronounceable non-words were generated using Wuggy software (Keuleers & Brysbaert, 2010).

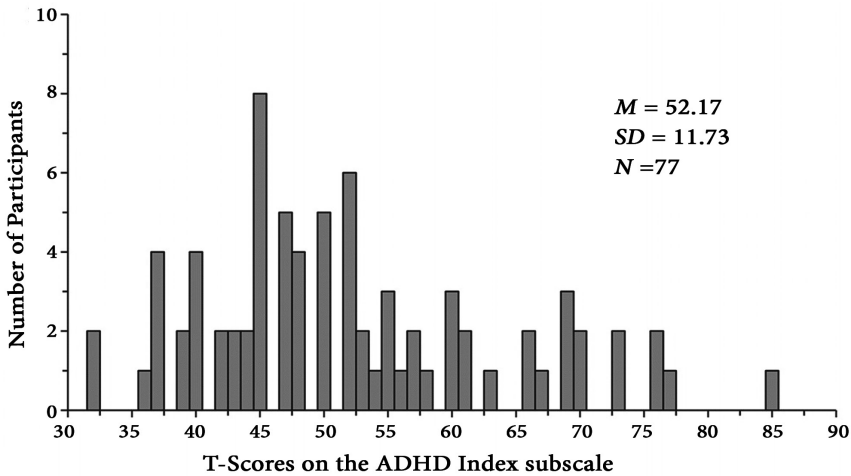


Figure 3.1. Distribution of the T-scores on the ADHD index subscale of the CAARS.

Stimuli consisted of two different horizontal letter-strings of same length (three, four, and five letters long) presented bilaterally in lower-case, one letter-string in each visual field. The innermost edge of each letter-string was located at  $1.23^\circ$  to the left or right of a central fixation cross. State regulation was manipulated by three event rates with inter-stimulus-interval of 2000, 4200, and 8200 ms. Inter-stimulus-intervals were derived from the only available meta-analysis on event rate effects on task performance (Metin et al., 2012). Each event rate condition lasted approximately 15 minutes with 384 trials for the fast, 192 trials for the medium and 96 trials for the slow event rate. In each event rate, trials were randomised for visual field (LVF, RVF), wordness (words, non-words), and word frequency (high, low frequency) of both the target and distracter. Participants responded in each condition with their right hand for half of the trials and with their left hand for the other half. The order of responding hand and the three event rates were counterbalanced across the participants. The trial started with a fixation cross presented in the centre of the screen for 200 ms followed by two letter strings presented bilaterally for 150 ms. Finally, a fixation cross presented for 1800, 4000 or 8000 ms depending on the event rate condition.



For each participant, mean RTs and performance accuracy were calculated for the target's visual field, wordness and word frequency, regardless of the distracter. Performance accuracy was calculated as the number of correct responses of one condition divided by the number of trials of the same condition. In each event rate condition, brain laterality was measured in terms of visual field advantage (faster and more accurate performance for one visual field above the other). For mean RTs, the size of visual field advantage was calculated for target words and target non-words apart by applying the following formula:  $(LVF - RVF)$ . Similarly, for performance accuracy the size of visual field advantage was calculated by:  $(RVF - LVF)$ . Given the fact that stimuli presented in one visual field are initially processed by the contralateral hemisphere, a larger size of visual field advantage (positive value) was taken to reflect faster and more accurate processing in the left hemisphere relative to the right hemisphere.

### Procedure

The study had two sessions: in the first, the participants had one hour to fill in the CAARS in group testing. They were instructed to rate how well the items of the questionnaire applied to themselves on a 4-point scale. It was emphasized that the questionnaire had to be answered as accurately as possible. In the second session, the participants were tested individually on the lateralized lexical decision task. The participants were seated in a dimly lit room behind a table on which the laptop was positioned. The use of medication and vision and motor problems of the participants were asked and noted. Before running the experiment, the participants were instructed to indicate whether the underlined stimulus was a word by pressing button '1' with index finger of one hand, or a non-word by pressing button '2' with middle finger of the same hand. The decisions had to be based on the participant's mother language. It was emphasized that: (1) They had to keep their gaze on the central fixation cross all the time and not to turn their gaze away when stimuli appeared, (2) To react as fast and accurately as possible to the underlined stimulus (the target), and to ignore the stimulus that was not underlined (the distracter), (3) That all letters would be displayed in lower-case, and (4) Anticipated eye blinks should be made directly after the response.

Halfway through each event rate condition, the task was stopped for few seconds to change the responding hand. Before each condition, a practice block of trials was given until seven out of ten consecutive responses were correct; thereafter, the actual task was started. The experimenter was present during testing sessions and monitored whether the subjects attended to the screen. To avoid physical discomfort and fatigue participants were allowed a rest period of five minutes between the three task conditions.

### Data analysis

To test the effect of event rate on task performance (the slower the event rate, the slower and more variable are RTs), repeated measures analyses of variance on overall mean of RTs, standard deviations of RTs (SDs), and performance accuracy were performed. The within-subject factor was Event Rate (fast, medium, or slow condition).

To examine the left hemisphere functioning and its relation to state regulation capacity, repeated measures analysis of variance was performed on the size of visual field advantage.

The within-subject factors were the wordness of the target (words or non-words) and event rate (fast, medium, or slow condition). Scores on the ADHD Index subscale of the CAARS were included in the analysis as a continuous independent variable to test whether the level of ADHD symptomatology affects the relation between left hemisphere functioning and state regulation. In the same manner, repeated measure analysis of variance was performed on the size of visual field advantage of high- versus low-frequency words in order to test whether a subtle deficit in the right hemisphere processing contributes to poor state regulation in ADHD symptomatology.

The dependent variable (the size of visual field advantage) was continuous and normally distributed in the fast, medium and slow condition as tested by Shapiro-Wilk Test ( $S-W = .97$ ,  $df = 77$ ,  $p = .21$  for the fast,  $S-W = .97$ ,  $df = 77$ ,  $p = .10$  for the medium,  $S-W = .98$ ,  $df = 77$ ,  $p = .28$  for the slow event rate).

## Results

### Task performance

For all participants, the event rate manipulation affected the overall RT performance. The mean RTs (mean SDs) for the fast, medium and slow event rates were respectively 693(172), 794(201) and 867 (209) ms. The slow performance and its increased variability from fast to slow event rate reflected a decreasing motor activation state, statistically confirmed by a significant main effect of event rate on mean RTs,  $F(1, 76) = 171.19$ ,  $p < .000$ ,  $\eta^2 = .69$ , and on mean SDs,  $F(1, 76) = 35.82$ ,  $p < .000$ ,  $\eta^2 = .32$ . Consequently, it may be concluded that the manipulation of event rate was effective as far as response speed and variability were concerned. Event rate did not influence percentage of correct responses ( $p = .63$ ). Correct responses in the fast, medium and slow conditions were respectively 82.1%, 83.3% and 81.6 %.

### The relation between brain laterality, state regulation, and the level of ADHD symptomatology

**Visual field advantage calculated from RTs measures.** Analyses on the size of visual field advantage revealed a higher RVF advantage for words ( $M = 28.5$  ms) than for non-words ( $M = 8.2$  ms) confirmed by a significant main effect of wordness,  $F(1, 75) = 8.46$ ,  $p = .005$ ,  $\eta^2 = .10$ . This finding indicates that words are processed faster in the left hemisphere relative to the right hemisphere compared to non-words.

The RVF advantage for words was higher when the event rate was slower. The size of RVF advantage for words was 15.5, 33.2, and 36.8 ms for the fast, medium and slow event rate, and resulted in a significant main effect of event rate,  $F(1, 75) = 8.848$ ,  $p = .004$ ,  $\eta^2 = .11$ . For non-words, the size of visual field advantage was unrelated to the event rate manipulation ( $p = .570$ ). These findings indicated that especially word processing lateralized to the left hemisphere was associated with the motor activation state of the subjects. The raw data of RTs per event rate, wordness, and visual field of the target is presented in table 3.1.

Table 3.1. Mean RTs and Accuracy (Percentage of Correct Responses) of the Left and Right Visual Field for Words and Non-words in the Three Event Rates.

Sample ( <i>N</i> = 77)	Fast ER				Medium ER				Slow ER					
	Non-words		Words		Non-words		Words		Non-words		Words			
	LVF	RVF	LVF	RVF	LVF	RVF	LVF	RVF	LVF	RVF	LVF	RVF		
	RT	<i>M</i>	741	742	660	644	858	840	765	732	933	926	835	798
	<i>SD</i>	99	96	85	85	130	121	109	103	178	171	145	142	
Accuracy	<i>M</i>	77%	79%	84%	87%	87%	78%	82%	83%	90%	75%	79%	82%	90%
	<i>SD</i>	10%	11%	10%	10%	10%	12%	10%	14%	8%	15%	13%	14%	10%

Note. ER = Event Rate; LVF = Left Visual Field; RVF = Right Visual Field.

Figure 3.2. suggests that the effect of event rate on the RVF advantage for words was modulated by ADHD scores. That is to say, overall, in the slow event rate the RVF advantage was the highest; however, subjects with higher ADHD scores had a reduced RVF advantage in the slow event rate. The suggestion was confirmed by the following analyses: the interaction between the ADHD Index scores, event rate, and wordness was both linearly,  $F(1, 75) = 4.91$ ,  $p = .030$ ,  $\eta^2 = .06$ , and quadratically,  $F(1, 75) = 5.91$ ,  $p = .017$ ,  $\eta^2 = .07$ , significant, see figure 3.2. Decomposing the interaction between event rate and ADHD Index scores into words and non-words revealed a significant interaction for words,  $F(1, 75) = 10.782$ ,  $p = .002$ ,  $\eta^2 = .13$ , but not for non-words ( $p = .59$ ).

For words, we followed up the significant main effect of event rate on the RVF advantage with Bonferroni corrected pairwise comparisons between the three event rates (the fast versus the medium rate, the fast versus the slow rate, and the medium versus the slow rate). To correct  $p$ -values using the Bonferroni correction method, we divided the desired significance level of .05 by the number of comparisons (three). Any comparison with  $p$ -value higher than .0167 was considered non-significant. The comparisons revealed that subjects with higher ADHD Index scores had a reduced RVF advantage for words in the slow event rate compared to the medium event rate: the interaction between ADHD Index scores and event rate was significant,  $F(1, 75) = 10.435$ ,  $p = .002$ ,  $\eta^2 = .12$ . Other comparisons between the fast and medium event rate and between the fast and slow event rate were not significant ( $p$  values  $\geq .031$ ). Pearson correlation test between the ADHD Index scores and the size of RVF advantage for words was significant for the slow rate ( $N = 77$ ,  $r = -.24$ ,  $p = .032$ ), but not for the fast ( $p = .493$ ) or for the medium rate ( $p = .130$ ).

With respect to the effect of word frequency on the visual field advantage, the analysis revealed that high frequency words tended to have lower size of visual field advantage ( $M = 16\text{ms}$ ) than low frequency words ( $M = 24\text{ms}$ ), the main effect of word frequency was  $F(1, 75) = 3.018$ ,  $p = .087$ ,  $\eta^2 = .04$ . This effect was not influenced by the event rate or ADHD Index scores: none of the interactions of word frequency with event rate and ADHD Index scores was significant ( $p \geq .156$ ).

**Visual field advantage calculated from percentage of correct responses.** Analyses on the size of visual field advantage showed no main effects of wordness of the target ( $p = .559$ ) and event rate ( $p = .420$ ). Neither the interaction between wordness and ADHD Index scores nor the interaction between wordness, ADHD Index scores, and event rate was significant ( $p \geq .211$ ). Percentages of correct responses per event rate, wordness and visual field of the target are shown in table 3.1. As can be seen from the table, in performance accuracy there is no shift in the differences between left and right visual field over the three event rate conditions, indicating the RVF-LVF accuracy balance over the three event rate conditions did not play a role in the similar overall accuracy between the three event rates (i.e., no interaction between the conditions and visual field).

With respect to the effect of word frequency, the high- and low-frequency words had similar visual field advantage as calculated from performance accuracy. This finding was similar for

the three event rates, and was not influenced by the scores on the ADHD index subscale: neither the main effect of word frequency nor its interaction with event rate was significant ( $p$  values  $\geq .632$ ). Also, the three-way interaction between word frequency, event rate, and ADHD Index scores was not significant ( $p = .254$ ).

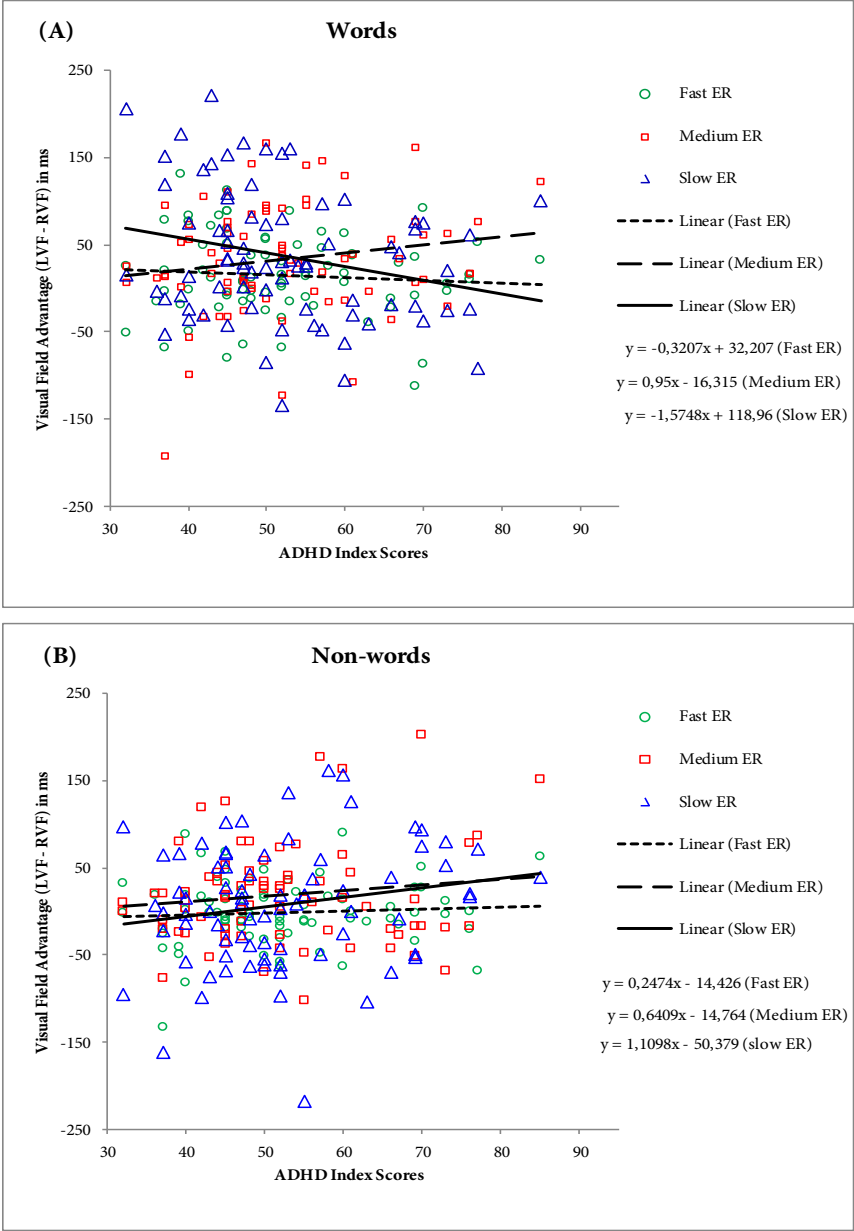


Figure 3.2. Scatterplots and linear relationship between the T-scores on the ADHD index subscale of the CAARS and the size of visual field advantage per event rate for words (A) and non-words (B). Note: ER = Event Rate.

## Discussion

The aim of the study was to investigate the link between state regulation, left hemisphere function, and ADHD symptomatology. The study achieved to explore left hemisphere functioning because event rate did not affect processing of non-words and high frequency words which tap the right hemisphere functioning. Since the event rate manipulation did not affect performance accuracy, this dependent variable is not taken into consideration any further. Before discussing the main findings, the task validity will be discussed because the present study is the first wherein a lexical decision task was combined with the event rate manipulation.

No drop in reaction time performance was observed in the fast condition compared to the medium one. This negative finding might be considered to be add odds with the cognitive-energetic model whereby an inverted U shape performance curve is expected. As has been put forward by Sanders (1983, 1998), task inefficiency during a fast presentation rate of stimuli occurs mainly in highly emotional or threatening conditions. There is little systematic evidence on the effects of flooding (too much energy supply) in a condition with a fast presentation rate. *Note: the only exception is the ADHD study by van der Meere, Shalev, Börger and Wiersema (1995). Here, the combination of methylphenidate and a fast presentation rate of stimuli resulted in task inefficiency in children with ADHD.* This may explain why the majority of state regulation studies in ADHD failed to report an inverted U shape performance curve and reported normal performance in the fast rate compared to the medium one. But in accord with the theory, the event rate manipulation resulted in the expected drop in response performance (response delay and increased response variability) in the slow condition, which has been explained in terms of inefficient effort allocation. All in all, event rate manipulation was effective to study lateral differences in visual field performance as far as the slow and medium condition were concerned.

At this point, the question emerges which process of the lexical decision task is affected by the event rate manipulation: the verbal or motor processes of the task? According to Sanders model (1983,1998) event rate loads on the motor activation component of any cognitive task. It is self-evident that the lexical decision task has a motor activation component: the prime brain area of the lexical decision performance, Broca's area in the left hemisphere, is involved in both language and motor functions (Binkofski & Buccino, 2004; Koechlin & Jubault, 2006). Consequently, the main finding that higher ADHD scores were associated with a reduced RVF advantage in the slow condition might be interpreted in terms of weak left hemisphere functioning to compensate the low motor activation due to less effort allocation (motivation). The link between motivation and the left hemispheric is also underlined by Rutherford and Lindell (2011). They showed that the left hemisphere is responsible for keeping humans motivated to perform the tasks via regulating the motor activity and emotions.

A growing body of research suggests that language and motor activity are highly interconnected (for a review see, Fischer & Zwaan, 2008). A recent study by Rueschemeyer, Lindemann, van Rooij, van Dam, and Bekkering (2010) showed that executing motor actions has a selective positive effect on word processing in a lexical decision task. They concluded that motor activation can have either inhibitory or facilitation effects on lexical processing.

Our finding that word processing was affected in the slow condition (low motor activation), but not in the medium condition might suggest that state regulation deficits may contribute to some extent to language impairments in ADHD (Bellani, Moretti, Perlini, & Brambilla, 2011; Bruce, Thernlund, & Nettelbladt, 2006). The reasoning is as follows: the present findings in combination with the earlier discussed fMRI state regulation study (Metin et al., 2015) suggest that the DMN activity increases in the left hemisphere, especially in the slow condition. This increased task-unrelated activity means that there is less task-related capacity to process linguistic information. Indeed, clinical ADHD studies showed a reduced task-related activity in the left hemisphere (Cubillo et al., 2010; Ernst, Zametkin, Matochik, Jons, & Cohen, 1998; Hart, Radua, Mataix-Cols, & Rubia, 2012; Sieg, Gaffney, Preston, & Hellings, 1995), and others showed impaired linguistic processing at the behavioural level in ADHD (Hale et al., 2005, 2008). Moreover, less task-related activity to process linguistic information might also compromise internalized speech, which is an important factor in executive functioning: a key in ADHD (Hervey, Epstein, & Curry, 2004). All in all, the present outcome shows that word processing is affected in subjects with higher levels of ADHD symptoms. The study of Hale et al. (2005) also indicated that adults with clinical ADHD diagnosis had problems in word recognition in a similar task as ours. Hale and colleagues questioned whether the word recognition deficit is caused by abnormal use of lateralized cognitive resource or by fundamental language impairments. Our study showed that there might be an additional motivational component in language impairments in ADHD: problems in regulating motor activation state may play a role in semantic processing deficits.

Notably, the concepts of arousal and activation are used interchangeably or, at times, are defined in different ways (Loo et al., 2009). For instance, arousal is often defined as the current energetic state of the subjects whereas activation is defined as a separable tonic measure of energy mobilization related to task performance (Vaez-Mousavi et al., 2007). Using the definitions of Pribram and McGuinness (1975) of arousal and activation, the data clearly indicates that the left hemisphere is involved in the regulation of motor activation, and that the left hemisphere might be compromised in subjects with elevated levels of ADHD symptomatology. Whether the right hemisphere is compromised in regulating the arousal was not part of the mission, and therefore not tested. To test right hemisphere function in regulating the arousal, a future study may be needed using visual spatial stimuli together with the presence or absence of (alarming) cues measuring arousal.

The study's outcome might contribute to an important topic in the field of ADHD: the development of ADHD. Follow-up studies show that a considerable percentage of children with ADHD grow out of their deficits (van Lieshout, Luman, Buitelaar, Rommelse, & Oosterlaan, 2013; Thissen et al., 2014). This could indicate that impairments in neurocognitive functioning in children do not underlie true ADHD, but may be epiphenomena. It has been proposed that as a function of age there is improvement in executive neuropsychological functioning, but compromised lower-order functioning, such as a state regulation deficit, remains stable over time (Halperin & Schulz, 2006; Halperin, Trampush, Miller, Marks, & Newcorn, 2008). This hypothesis is usually tested using tasks with high and low executive demands, and the research outcome is mixed (Coghill, Hayward, Rhodes, Grimmer, & Matthews, 2014). Our task consisted of a high executive component, i.e. lexical decision making, and a low executive



demand (state regulation). The adult sample, especially those with higher ADHD scores, showed an intact executive component together with a more pronounced deficit in the lower-order component (state regulation). These data highlight the importance of longitudinal studies on the development of executive functioning, state regulation, and brain laterality in remitters and persisters.

Finally, at present the state regulation hypothesis in ADHD is based on children and adults fulfilling the DSM criteria for ADHD. It is well recognized that research using clinical populations may have many confounders such as lower IQ, gender, co-morbidity, and variability in socioeconomic factors. Choosing university students might control to a high extent for these factors. Therefore, the present findings indicate that ADHD may represent a pure effort allocation deficit.

### **Limitation**

The present study is confined to right-handed adults. Moreover, the participating university student sample is not representative of adults in general; therefore, a replication is needed using broader defined samples. The study did not evaluate comorbidities related to ADHD such as dyslexia, a common disorder that affects lateralized lexical decision performance. However, we excluded subjects who reported learning disorders. In addition, learning disorders are supposed to be absent or minor in university students. The fact that task performance was intact in the fast stimulus presentation rate indicates that our fast rate did not provoke energy overflow and might not be considered a sufficient stressor to affect task performance. A future study may address how fast the task should be to induce over-activation.

### **Conclusions**

The study provides evidence that during the slow event rate adults with higher levels of self-reported ADHD symptoms have a reduced right visual field advantage compared to the medium event rate, indicating that the left hemisphere functioning is affected by the motor activation state. It might be concluded that impaired state regulation plays a role in left hemispheric functioning in ADHD.

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Post-error Slowing Accuracy Attention-Deficit/Hyperactivity Disorder Error Monitoring  
Difficulties in Allocating Effort to Protect Performance against Stressors the Left  
Hemisphere Right Lateralized Lexical Decision Task Improved Response Accuracy  
After Errors Response Strategy Error Processing Right Visual Field Left Visual Field  
Slow Presentation Rate of Stimuli Post-error Adjustments in ADHD In healthy Adults, the  
Left Hemisphere Is More Involved in Post-error Adjustments In healthy Adults  
Post-error Slowing Is Stronger During Slower Stimulus Presentation Rate Adults with  
High ADHD Scores Have NO Post-error adjustments As Healthy Adults, Which Half of  
the Brain Is Responsible for Poor Error Monitoring in Adults Who Report High Level of  
ADHD Symptoms ? Error detection Is Intact When the Presentation Rate is Fast, But It  
Drops When the Presentation Rate Is Slow Error Characteristics in ADHD An Orienting  
Account Malfunctioning Processes Lead to An Error on the Previous Trial

